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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/502,283	02/11/2000	Sun Ai Raillard	02-029510US	4948

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/502,283	RAILLARD ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6,23-26,72,73,77,78,106-109,115-119 and 125-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6,23-26,72,73,77,78,106-109,115-119 and 125-144* is/are rejected.

7)☒ Claim(s) *115* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on December 26, 2006 has been entered.

2. Claims 3-6, 23-26, 72, 73, 77, 78, 106-110, 115-119 and 125-143 were pending. Applicants canceled claim 110, added claim 144 and amended claim 136. Therefore, claims 3-6, 23-26, 72, 73, 77, 78, 106-109, 115-119 and 125-144 are currently pending and examined on the merits.

IDS

3. The information disclosure statement filed December 4, 2000, fails, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because many publication(s) cited therein, lack publication dates, titles, page numbers, journal references (e.g., see references AI-AN, AQ-AY, and BA-BO). While the other patent and other publications cited therein, and supplied, therewith, have been considered as to the merits, the above cited publications have not. Applicant is advised that the date of any re-submission of these citations contained in this information disclosure statement or the submission of the missing element – their publication

dates – will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPE § 609 C(1).

Priority/Specification

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) and/or 120 as follows:

This application claims benefit of and priority to USSN 60/119,766, "High Throughput Mass Spectrometry," by Raillard; USSN 60/148,848 entitled "Evolution and Use of Enzymes for Combinatorial and Medicinal Chemistry," by Liu et al., filed August 12, 1999, and co-filed PCT application, "High Throughput Mass Spectrometry," by Raillard et al., filed February 11, 2000, PCT/US00/03686 (e.g., see 12/26/06 amendment to specification). However, one or more of the applications stated above fail to provide adequate support under 35 U.S.C. § 112, first paragraph for the claimed invention as follows:

> (A) For ***claims 3-6, 23-26, 72, 73, 77, 78, 106-109, 115-119 and 125-144***, all priority documents fail to provide support for the new matter listed below (e.g., see 35 U.S.C. § 112, first paragraph rejection below, which is incorporated in its entirety herein by reference).
>
> (B) For ***claims 4-6, 23-25, 78, 116, 118, 126***, the '766 application additionally fails to provide support for "neutral" loss mass spectrometry in claims 23-25, 116 and 118. The '766 application also fails to provide support for "pooling" samples as set forth in claims 78 and 126. The '766 application also fails to disclose sample rates > 100/hour as set forth, for example, in claims 4-6.
>
> (C) For ***claims 3-6, 23-26, 72, 73, 77, 78, 106-109, 115-119 and 125-144***, the '848 application additionally fails to provide support for "tandem" mass spectrometry as recited in independent claims 127 and 136 (and their corresponding dependent claims). The '848 application also fails to provide support for the "carbohydrate" analytes recited in independent claim 127. The '848 application also fails to provide support for the volatile buffers as set forth in claims 134 and 143.

If applicant believes this assessment is in error, applicant must disclose where in the specification support for these limitations can be found. See MPEP § 714.02. Therefore the filing date of the instant application is deemed to be its actual filing date, **February 11, 2000**.

5. In addition, if applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. § 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an

unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Here, Applicants fail to set forth the "relationship" (i.e., continuation, continuation-in-part, etc.) for the PCT/US00/03686 (e.g., see 12/26/06 amendment to the specification, "The present application claims benefit of ... PCT/US00/03686). The passage also fails to provide the filing date for the '766 provisional application.

New Rejections/Objections

Objections to the Claims

6. Claim 115 is objected to because of the following informalities:

A. Claim 115 incorrectly recites "claim136" in line 1. Correction is requested.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 144 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. **Claim 144** recites the limitation "the component(s) of interest" in line 1. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 144 and all dependent claims are rejected under 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 3-6, 23-26, 72, 73, 77, 78, 106-109, 115-119 and 125-144 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Independent claims 127 and 136 were amended and/or added in the 8/29/05 response to include the limitation "wherein the components of interest has not undergone chromatographic separation prior to step (iv)" in conjunction with the limitation "using centrifugation or filtration in parallel fashion" to separate the cells or cell debris from the component of interest. However, Applicants cited passages (e.g., see 8/29/05 response, pages 9 and 10 wherein Applicants provide reference to various passages that allegedly provide support for those amendments) do not provide support for separating cells or cell debris using "only" centrifugation and/or filtration for "any" analyte and to the extent that Applicants' claims read on such embodiments such scope represents new matter. For example, the specification reads, "Effective sample cleanup is dependent on the physico-chemical nature of the analyte as well as the matrix" (e.g., see specification, paragraph bridging pages 32 and 33). Accordingly, several strategies are set forth for separating cells and/or cell debris depending on the nature of the analyte/matrix including Applicants' currently claimed centrifugation/filtration combination for small molecule substrates like atrazine (e.g., see page 33, first full paragraph), cation exchange resin for small inorganic ion analytes (e.g., see page 33, second full paragraph), a combination of exchange resin, ethanol precipitation, and filtration for oligosaccharide analytes (e.g., see page 33, third full paragraph), and aqueous phase organic solvents for analytes like polyketides (e.g., see page 33, fourth full paragraph). Other methods set forth include the use of tag binding techniques for separation of enzymes, proteins, nucleic acids, etc. (e.g.,

see page 4, second full paragraph). Thus, use of Applicants' currently claimed centrifugation/filtration technique in the absence of chromatographic separation is not universally applied to all of the claimed analytes as set forth above. Therefore, claim 127, 137 and all-dependent claims represent new matter.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 3, 72, 73, 77, 78, 106, 125-134, 136-144 are rejected under 35 U.S.C. 102(e) as being anticipated by Stemmer et al. (U.S. Patent No. 6,500,617 B1) (Filed **April 22, 1999**) as evidenced by provisional application 60/119,766 (filed **February 11, 1999**).

For ***claims 72, 73, 127, 136, 141, and 142***, Stemmer et al. (see entire document) disclose a method of performing high throughput mass spectrometry screening (e.g., see column 53, second full paragraph, "A high throughput method for detecting analyte molecules from a complex biological matrix is by electrospray tandem mass spectrometry"). Furthermore, Stemmer et al. disclose a method that comprises providing cells that have been transfected or transformed with one or more members of library of related genes (e.g., see column 53, first full paragraph, "In one aspect, library members

e.g., cells ... produce individual colonies ... and 10,000 different mutants inoculated into 96 well microtiter dishes"). In addition, Stemmer et al. disclose growing the cells in vitro in biological matrix to express said members of the library of related genes (e.g., see column 53, first full paragraph disclosing "culture medium" as the matrix; see also column 46, line 36; see also Example 10, especially lines 50-62, "pools of the transformed cells are grown in each well). In addition, Stemmer et al. disclose separating the cells or cell debris thereof from one or more component of interest using centrifugation or filtration in parallel fashion to provide samples (e.g., see column 53, second full paragraph disclosing the filtration/centrifugation method set forth in the '766 Raillard application; e.g., see also '766 application, pages 21-23, section VI; especially page 22, paragraphs 1-3; disclosing filtration and/or centrifugation techniques). Stemmer et al. also disclose performing flow injection analysis using electrospray tandem mass spectrometry on the samples from step iii to obtain mass to charge ratio data for the component of interest wherein the component of interest (e.g., see column 53, second full paragraph). In addition, Stemmer et al. also disclose a component use of a component of interest selected from the group consisting of an inorganic ion, secondary metabolite, protein binding molecule, carbohydrate, carbohydrate binding molecule, an enzyme, an enzyme substrate product of an enzyme catalyzed reaction, nucleic acid and product of nucleic acid catalyzed reaction (e.g., see Example 7 wherein a protease inhibitor i.e., a protein binding molecule is disclosed; see also abstract and examples wherein "protein binding" toxin molecules are disclosed). Finally, Stemmer et al. disclose methods wherein the component of interest has not undergone chromatographic separation prior to

step iv (e.g., see Example 10; see also column 53, second full paragraph; see also '766 application, section VI as noted above; see also summary of invention). In addition, Stemmer et al. disclose providing cells that have been transfected or transformed with one or more members of library of related enzyme encoding genes (e.g., see column 33, line 54; see also column 51, line 38).

For ***claims 3, 77, 106, and 125***, Stemmer et al. disclose at least about 100 samples are screened for presence of the one or more component of interest in less than an hour (e.g., see column 53, second full paragraph wherein the '766 method is disclosed; see also '766 application, page 3, line 15; see also page 5, line 23; see also page 32, line 4; see also claim 24).

For ***claims 78 and 126***, Stemmer et al. disclose to 100 samples are pooled before performing flow injection analysis using electrospray tandem mass spectrometry (e.g., see Stemmer et al., lines 46-48).

For ***claims 128 and 137***, Stemmer et al. disclose the cells are lysed prior to step iii (e.g., see Example 1, especially, column 54, line 67).

For ***claims 129 and 138***, Stemmer et al. disclose the cells are permeabilized prior to step iii permeabilized prior to step iii (e.g., see column 53, lines 27-35; also '766 application, page 20, line 19).

For ***claim 130 and 144***, Stemmer et al. disclose the component of interest is obtained from cell supernatant (e.g., see Stemmer et al., column 37, line 57; see also Example 7, especially column 59, line 32, "After cell debris is removed by

centrifugation, the supernatant is used as the protease preparation without further purification"; see also Example 8; see also '766 application, line 12).

For ***claim 131***, Stemmer et al. disclose the component of interest is product of an enzymatic reaction (e.g., see Stemmer et al., column 41, wherein library initially produced by restriction enzymes).

For ***claim 132 and 139***, Stemmer et al. disclose the cells are bacterial cells (e.g., see column 46, paragraph 1 wherein a variety of host cells are disclosed).

For ***claim 133 and 140***, Stemmer et al. disclose the cells are eukaryotic cells (e.g., see column 46, paragraph 1 wherein a variety of host cells are disclosed).

For ***claim 134 and 143***, Stemmer et al. disclose step iii is performed in volatile buffer, a buffer that reduces concentration of ionic species, or an organic solvent (e.g., see column 53, lines 27-35; see also '766 application, page 22, line 11, page 31, line 10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 3-6, 23-26, 72, 73, 77, 78, 106-109, 115-119 and 125-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer et al. (U.S. Patent No. 6,500,617 B1) (Filed **April 22, 1999**) in view of Favretto et al. (Fabretto et al. "MS/MS applications in biological problems" Mass Spectrometry Reviews **1993**, *12*, 313-395) as evidenced by provisional application 60/119,766 (filed **February 11, 1999**)

For ***claims 3, 72, 73, 77, 78, 106, 125-134, and 136-144***, Stemmer et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 3, 7, 72, 73, 78, 106, 125-134, and 136-144. *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983) ("anticipation is the epitome of obviousness"); see also *In re Skoner*, 517 F.2d 947, 950, 186 USPQ 80, 83 (CCPA 1975); *In re Pearson*, 494 F.2d 1399, 1402, 181 USPQ 641, 644 (CCPA 1974).

The prior art teaching of Stemmer et al. differ from the claimed invention as follows:

For ***claims 4-6 and 107-109***, Stemmer et al. fail to disclose at least about 200, 500, or 1000 samples are screened for presence of the one or more component of interest in less than an hour/day. Stemmer et al. only disclose 100 samples/hour (see above). However, 100 samples hour would equate to 2,400 samples/day if allowed to run for a

24-hour period, which would render obvious claims 6 and 109. In addition, the Examiner notes "the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA1955). Also note that optimization of process steps, especially with respect to numbers of samples analyzed or numbers of substrate regions is within the routine skill of the art. *In re Burhans*, 154 F.2d 690, 69 USPQ330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results). With respect to the repetition of steps (i.e. number of samples analyzed or number of substrate regions), see *In re Harza*, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. Here, the mere increase in sample rate would not be inventive absent some showing of unexpected results.

For ***claims 23 and 116***, Stemmer et al. fail to disclose performing flow injection analysis using electrospray tandem mass spectrometry performing method selected from the group consisting of neutral loss mass spectrometry and parent ion mass spectrometry

For ***claims 24 and 117***, Stemmer et al. fail to disclose comprising performing the neutral loss mass spectrometry or the parent ion mass spectrometry on triple quadrupole mass spectrometer

For ***claim 25***, Stemmer et al. fail to disclose performing the neutral loss mass spectrometry scanning the one or more component of interest in first quadrupole at specified mass range fragmenting the one or more component of interest in second

quadrupole by collision induced dissociation thereby producing one or more neutral fragments and one or more daughter ion and detecting the one or more daughter ion

For ***claim 26***, Stemmer et al. fail to disclose performing the parent ion mass spectrometry scanning the one or more component of interest in first quadrupole fragmenting the one or more component of interest in second quadrupole by collision induced dissociation and scanning third quadrupole at specified mass

For ***claims 115 and 135***, Stemmer et al. fail to disclose simultaneously quantifying the amount of the product of an enzyme reaction and the enzyme substrate

For ***claim 118***, Stemmer et al. fail to disclose performing the neutral loss mass spectrometry scanning the product of the enzymatic reaction and/or enzyme substrate in first quadrupole at specified mass range fragmenting the product of the enzymatic reaction and/or enzyme substrate in second quadrupole by collision induced dissociation thereby producing one or more neutral Fragments and one or more daughter ion and detecting the one or more daughter ion

For ***claim 119***, Stemmer et al. fail to disclose performing the parent ion mass spectrometry scanning the product of the enzymatic reaction and/or enzyme substrate in first quadrupole fragmenting the product of the enzymatic reaction and/or enzyme substrate in second quadrupole by collision induced dissociation and scanning third quadrupole at specified mass

However, Favretto et al. teach the following limitations that are deficient in Stemmer et al.:

For ***claim 23 and 116***, Favretto et al. disclose performing flow injection analysis using electrospray tandem mass spectrometry performing method selected from the group consisting of neutral loss mass spectrometry and parent ion mass spectrometry (e.g., see page 320, last paragraph; se also page 333, first full paragraph; see also page 338, first paragraph; see also figure 16; see also page 339, first full paragraph; see also page 342, last paragraph; see also page 343, first full paragraph; see also page 348, second to last paragraph; see also page 355, Pharmacology and Toxicology section; see also Lipid section starting on page 362; see also page 365, Hybrid Instruments section; see also Table II, etc. wherein "neutral loss" is disclosed).

For ***claims 24 and 117***, Favretto et al. disclose comprising performing the neutral loss mass spectrometry or the parent ion mass spectrometry on triple quadrupole mass spectrometer (e.g., see page 322-325, starting with "Triple Quadrupole Instruments" section; see also page 351, second full paragraph; see also page 354, Nucleic Acids Constituents section; see also page 380, paragraph 1, etc.).

For ***claims 25, 26, 118, 119***, Favretto et al. disclose performing the neutral loss mass spectrometry scanning the one or more component of interest in first quadrupole at specified mass range fragmenting the one or more component of interest in second quadrupole by collision induced dissociation thereby producing one or more neutral fragments and one or more daughter ion and detecting the one or more daughter ion (e.g., see page 345, second paragraph in Natural Products section, MS/MS analyses ... under different conditions (FAB, DCI, low- and high-energy CID"; see also page 359, second

full paragraph; see also page 368, paragraph 1; see also Triple Quadrupole Instruments" section noted above).

For ***claims 115 and 135***, Favretto et al. disclose comprising simultaneously quantifying the amount of the product of an enzyme reaction and the enzyme substrate (e.g., see page 341, third full paragraph; see also page 343, first full paragraph; see also page 344, paragraph 4; see also page 345, paragraph 1; see also page 350, third full paragraph; see also page 369, second full paragraph wherein a wide variety of analytes have been shown to be routinely "quantified" using these techniques).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use "neutral loss" techniques disclosed by Favretto et al. to examined the libraries as set forth by Stemmer et al. because Favretto et al. explicitly state that their MS/MS applications can be used in biological systems (e.g., see title and introduction), which would include the proteins and/or ligand disclosed by Stemmer et al. Furthermore, a person of ordinary skill in the art would have been motivated use these "neutral loss" techniques because Favretto et al. state that this technique is particularly valuable for the identification of analytes in "complex mixtures" (e.g., see Favretto et al., page 333, first full paragraph). The "neutral loss" technique also reveals functionalities and/or substructures of the original analyte for in depth characterization (e.g., see Favretto et al., page 338, paragraph 1). Finally, a person of ordinary skill in the art would reasonably have expected to be successful because Favretto et al. state that these techniques can be applied to biological systems including proteins, peptides, nucleic acids, lipids and small molecules (e.g., see Favretto et al., "Peptides" section starting on

page 367). In addition, many instruments with high resolution and sensitivity are available (e.g., see "Hybrid Instruments" section starting on page 365).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
March 27, 2007

JON EPPERSON
PRIMARY EXAMINER